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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,776	10/10/2001	Zhiwei Jiang	22596-514 (CO-14)	9481

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EXAMINER	
KRASS, FREDERICK F	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/975,776	JIANG ET AL.	
	Examiner	Art Unit	
	Frederick F. Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6, 9, 11, 12, 15, 18, 19, 21, 22, 25, 28, 30-34, 36, 37, 40, 43, 45-48, 51, 54, 180, 182-186 and 204-209* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,6,9,11,12,15,18,19,21,22,25,28,30-34,36,37,40,43,45-48,51,54,180,182-186 and 204-209.

Status of Case

Since the new ground of rejection which follows hereinunder was not necessitated by Applicant's amendment, this action is NON-FINAL.

Claim Informalities

The examiner notes that the recitation in claims 1, 11, 21, 31, 45, 180 and 204-209 specifying that the carrier molecule "is beta cyclodextrin" is, strictly speaking, inaccurate. The term is not considered indefinite *per se*, since the skilled artisan will be able to determine the claim scope, but what applicant really means is "a beta cyclodextrin", i.e. a genus. As currently constructed, "is beta cyclodextrin" obliquely implies that one particular species is being recited. This is, again strictly speaking, inconsistent with the recitation of the particular species "hydroxypropyl-beta-cyclodextrin" in various dependent claims, e.g. claim 6.

Accordingly, the examiner requests that Applicant place the claims in better form by inserting the word "a" before "beta cyclodextrin" in claims 1, 11, 21, 31, 45, 180 and 204-209.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 6, 9, 11, 12, 15, 18, 19, 21, 22, 25, 28, 30-34, 36, 37, 40, 43, 45-48, 51, 54, 180, 182-186 and 204-209 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pardee (WO 00/61142), taken in view of Bodor (USP 4,983,586).

The primary reference discloses the use of combinations of a) B-lapachone, or derivatives or analogs thereof, and b) G2/M drugs such as taxol/taxotere to treat cancer. Dosages range from 0.1 mg/kg to 50 mg/kg (see the last full paragraph at page 17) and the drugs may be separated into individual vials as parts of kits (page 20, first full paragraph on the page). Administration is by any of a variety of known routes, including parenteral (page 11, third paragraph). The reference recognizes that B-lapachone is insoluble in water (page 21, ninth and tenth lines), but differs from the instant claims insofar as it is silent regarding using a beta-cyclodextrin as a solublizing agent.

The secondary reference teaches that Applicant's preferred beta-cyclodextrin, hydroxypropyl-beta-cyclodextrin (see, e.g., instant claim 6), is useful for solubilizing a wide variety of water-insoluble drugs by complexation, particularly antineoplastic/antitumor agents. See col. 14, lines 20-27 and 50-55, for example. By

complexing the drugs with hydroxypropyl-beta-cyclodextrin, parenteral compositions which can be freeze-dried and reconstituted in water can be prepared therefrom. See the abstract, and lines 59-61 of col. 67, for example.

The secondary reference differs from the instant claims in that, although it teaches a wide variety of drugs, it does not specifically disclose B-lapachone, its analogs or derivatives. It does however, clearly teach that determining the suitability of a given drug for complexation with hydroxypropyl-beta-cyclodextrin is merely a matter of routine experimentation. As stated at col. 75, lines 40-47:

> Drugs which are particularly useful in the parenteral compositions and methods of the present invention are those which are relatively insoluble in water but whose water solubility can be substantially improved by formulation with 20 to 50% HPCD in water. These characteristics can be determined by simple experiments of the type described below for representative drugs.

B-lapachone, and its derivatives and analogs, are just such drugs, as is clear from the ninth and tenth lines of page 21 of the primary reference. Accordingly, it would have been obvious to have solubilized the antineoplastic/antitumor agents of the primary reference by complexing them with hydroxypropyl-beta-cyclodextrin, motivated by the desire to improve solubility for parenteral administration, as taught by the secondary reference. A solubility of at least 1mg/ml, as required by various dependent claims of the instant application (e.g. claim 9), would be reasonably expected given that 1) solubility can be "substantially improved" by HPCD, as noted in the above citation from the secondary reference and 2) once solubilized, B-lapachone can reach far higher levels than 1mg/ml, i.e. 20mg/ml as is clear from the disclosure of the primary reference at page 21, lines 11-13.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 6:30-3:00PM;
Tuesday: 10-6:30PM;
Wednesday: off;
Thursday: 10-6:30PM; and
Friday: 10-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Seidel Marianne, can be reached on 571-272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614